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| 10/564,311 | 01/11/2006 | Hidehito Kotani | BY0027P | 7112 |

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| EXAMINER | |
|---|---|
| ZARA, JANE J | |

| ART UNIT | PAPER NUMBER |
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| 1635 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/564,311 | KOTANI ET AL. | |
| | Examiner | Art Unit | |
| | Jane Zara | 1635 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1 and 22-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 22-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

This Office action is in response to the communication filed 4-7-08.

Claims 1, and 22-24 are pending in the instant application.

### *Response to Arguments and Amendments*

*Withdrawn Rejections*

Any rejections not repeated in this Office action are hereby withdrawn.

*Maintained Rejections*

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moon et al (J. Biol. Chem., Vol. 276, No. 48, pages 45,358-45,366, 2001) in view of Matsuzaka et al (J. Lipid Res., Vol. 43, pages 911-920, 2002) for the reasons of record set forth in the Office action mailed 1-3-08, and for the reasons set forth below.

Applicant's arguments filed 4-7-08 have been fully considered but they are not fully persuasive. Applicant argues that the teachings of Moon and Matsuzaka do not render the instant invention obvious because neither Moon nor Matsuzaka discloses or suggests that observations were made between weight change and LCE expression/activity in mice, nor is any connection between LCE and obesity specifically disclosed. Applicant also cites other references that had previously disclosed increased expression of various genes in the liver of obese mice, but have not been found to have a fixed correlation between increased expression and affects on body weight.

Applicant concedes, and is correct that Matsuzaka observed that cells overexpressing LCE showed high activity of fatty acid elongation and increased LCE expression in the liver of SREBP transgenic mice. But, contrary to Applicant's assertions, the combined teachings of Moon and Matsuzaka do render the instant invention obvious for several reasons. Matsuzaka teaches the role of elongase enzymes in lipogenesis. Matsuzaka teaches assaying long chain fatty acyl elongase protein activity in the presence of NADPH, palmitoyl CoA and labeled malonyl-CoA, as instantly claimed. What's more, on page 918, in the first full paragraph, Matsuzaka discloses:

> Leptin deficient mice (ob/ob) are an excellent murine model for obesity, insulin resistance, and diabetes. Previous studies indicate that the mRNA level of SREBP-1 and SREBP target genes involved in fatty acid biosyntheses were significantly elevated in livers from ob/ob mice compared with wild-type mice... We examined FACE mRNA levels in livers and WAT by Northern blot analysis. As shown in Fig. 8A, hepatic mRNA levels of FACE and SREBP-1 from ob/ob mice fed ad libitum were elevated compared with their respective wild-type controls.

Contrary to Applicant's assertions, Matsuzaka teaches the significance of their biochemical findings with respect to the motivation to study the inhibition of this enzyme in approaches to study obesity (second to last full paragraph of the discussion on page 919):

> Our current study established that FACE is a new member of the lipogenic enzyme family, based upon its fatty acyl elongation activity, SFEBP activation, and lipogenic regulation in numerous diet studies, such as overshooting induction at refeeding and PUFA suppression. Theoretically, the role of FACE in lipogenesis seems crucial because no other known enzymes have been reported to show the same activity as observed in this enzyme. However, the importance of this gene in lipogenesis as an energy storage system or in more basal cellular functions awaits analysis of effects of the FACE gene disruption…

And again the relevance of studying FACE in relation to human obesity is clearly articulated in the last paragraph of the discussion, page 919:

> It was reported that elongase activity estimated by C18:0-C16:0 ratio in the muscle is significantly related to adiposity in humans, suggesting that **FACE could be related to human obesity. Further studies might unveil clinical relevance of FACE to human diseases or pathophysiological states.**

(references omitted) (emphasis added].

Applicant concedes, and is correct that Moon teaches the high expression of LCE mRNA in liver and adipose tissue. But, contrary to Applicant's assertions, Moon also discusses their findings within the context of how LCE is possibly involved in obesity or weight gain:

> To search for targets of each SREBP in vivo, we previously produced lines of transgenic mice that overexpressed each SREBP isoform in liver. SFEBP-1a (TgSREBP-1a) transgenic mice **manifested large fatty livers**, owing to marked increases in mRNAs encoding lipogenic enzymes...

(see last full paragraph on p. 45,358) (citations omitted) (emphasis added).

It therefore would have been obvious to one of ordinary skill in the art to screen for inhibitors of LCE enzymatic activity because the enzyme had been cloned, recombinantly expressed, and an activity assay using the reagents instantly claimed had been developed previously by Moon and Matsuzaka. One of ordinary skill would have been motivated to screen for inhibitors of LCE enzyme activity in order to screen for candidate inhibitors of obesity or weight gain, because LCE had been identified as a lipogenic protein, and screening for inhibitors of LCE activity would have provided likely candidates for inhibiting the elongase activity, thereby inhibiting the increase in fatty compositions of liver, and potentially inhibiting lipogenic enzyme activity that is required in the obese state. The motivation to study the role of LCE activity in relation to obesity (and hence, weight gain) is clear, and the search for inhibitors of LCE activity would have been a logical choice in pursuing potential candidates for controlling weight gain, due to the observed relationship between LCE activity and lipogenesis repeatedly stated by both Moon and Natsuzaka.

One of ordinary skill in the art would have had a reasonable expectation of success in identifying candidate inhibitors of LCE activity by utilizing the routine assay protocols set forth by both Moon and Matsuzaka, and comparing the LCE activity in the absence and presence of candidate compounds, and since this enzyme was known to increase fatty compositions in the liver, one would have a reasonable expectation that finding an inhibitor of LCE activity would also provide a potential candidate for inhibiting obesity or weight gain in vivo. for these reasons, the instant rejection is maintained.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94

(December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jane Zara whose telephone number is (571) 272-0765. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz, can be reached on (571) 272-0763. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

**Jane Zara**
**6-27-08**
/Jane Zara/
Primary Examiner, Art Unit 1635